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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,699	03/30/2001	Munehide Kano	50026/022002	7451

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EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,699	KANO ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 7/24/06.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2,4,5,7,9,11-20,24,26,28-33,37,39,41-45 and 62-72 is/are pending in the application.

4a) Of the above claim(s) 46-61 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 2,4,5,7,9,11-20,24,26,28-33,37,39,41-45 and 62-72 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 30 March 2001 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 7/31/03, 7/24/06.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 24, 2006 has been entered.

Claims 1 and 3 have been canceled. Claims 2, 5, 11, 16, 17, 20, 24, 33 have been amended. Claims 67-72 are newly submitted. Claims 2, 4, 5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 41-45, 62-72 are under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 7/24/06 response would be addressed to the extent that they apply to current rejection.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 7/31/2003, and 7/24/2006 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. However, the U.S. patent applications as listed are not suitable for publication in the face of a patent.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 67-71 are rejected under 35 U.S.C. 112 first paragraph, because the specification as originally filed does not describe the invention as now claimed. The original disclosure fails to specify, "the part is a processed product" as now claimed. The term is now considered to be new matter.

In the Remarks, applicant points to page 22, lines 26-28 as support for the new claim language. However, it is noted the cited text of the specification (page 23 of record) states, "*SeV vector is constructed so as to express the full length of any of these virus proteins, including processed and unprocessed proteins, a part of them, or a combination of them*" (emphasis added). Here, the processed protein does not appear to be a part of the protein. Further, the recitation "a processed product" in the claims is not limited to a processed protein. Accordingly, the amendment is a departure or addition to the specification as filed, and it introduced new matter to the disclosure.

MPEP 2163.06 notes "WHENEVER THE ISSUE ARISES, THE FUNDAMENTAL FACTUAL INQUIRY IS WHETHER A CLAIM DEFINES AN INVENTION THAT IS CLEARLY CONVEYED TO THOSE SKILLED IN THE ART AT THE TIME THE APPLICATION WAS FILED...IF A CLAIM IS AMENDED TO INCLUDE SUBJECT MATTER, LIMITATIONS, OR TERMINOLOGY NOT PRESENT IN THE APPLICATION AS FILED, INVOLVING A DEPARTURE FROM, ADDITION TO, OR DELETION FROM THE DISCLOSURE OF THE APPLICATION AS FILED, THE EXAMINER SHOULD CONCLUDE THAT THE CLAIMED SUBJECT MATTER IS NOT DESCRIBED IN

THAT APPLICATION". MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED".

For reasons set forth above, the amendment filed 7/24/06 is objected to under 35 U.S.C. §132 because it introduces new matter into the disclosure. 35 U.S.C. §132 states that no amendment shall introduce new matter into the disclosure of the invention. Applicant is required to cancel the new matter in the reply to this Office Action.

The previous rejection of Claims 1-5, 7, 9, 11-20, 24, 26, 28-33, 37, 39, 41-45, 62-66 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in view of claim amendment, exhibit 1, and persuasive argument. Certain issues remain are currently addressed as lacking enablement (see rejection that follows).

Claims 20, 24, 26, 28, 30-33, 37, 39, 41, 43-45, 63-72 stand or newly rejected under 35 U.S.C. 112, first paragraph, because the specification supplemented by the state of the art, while being enabling for vaccination by intranasal administering a sendai virus vector expressing a protein of an immunodeficiency virus selected from the group consisting of Gag, Pol, gp41, Gag-pol, does not reasonably provide enablement for achieving a vaccine effect by intranasal administering a sendai viral vector expressing tat rev, vap, vpx, vpr, vif, nef proteins, and any parts of an immunodeficiency virus

protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims, for reasons of record and following.

In the Remarks, the applicant asserts that current claims included in this rejection do not recite the use of a Sendai virus vector as a vaccine, and clearly enabled.

In response, in light of the specification, the sole purpose of 'inducing an immune response specific to a virus protein of an immunodeficiency virus in an animal' is to reduce HIV/SIV virus replication, and claim 72 clearly recites "reducing setpoint plasma viral loads of an immunodeficiency virus in an animal", which requires a vaccine effect, and thus claims are evaluated according to such standard.

Concerning the type of immunodeficiency proteins, the applicant particularly argued over the *Matano* (AIDS 2003) reference.

In response, since contradictory evidence is abundant in the prior art, it is applicant's responsibility to provide an enabling disclosure for what is now claimed. For example, the applicant argues that the Office focuses on one negative result instead of two positive results of *Matano* (AIDS 2003), who investigated the vaccine effect of the tat protein.

In response, this is because the presence of contradictory evidence which can be found not only in *Matano* reference, but also in *Allen* (J Virol 2002, IDS) reference, who clearly teach despite the induction of tat-specific CTL, there was no significant reduction in either peak or viral set point compared to controls (e.g. abstract), and thus no protective effect on viral infection as should a vaccine.

Other earlier submitted references are insufficient to support the full scope of the claims for reasons of record reiterated following:

b. *Leung et al* disclosed recombinant BCG expressing gag, pol, env and nef of SIV/HIV proteins. The reference does not support the use of SeV-nef as a vaccine because *Leung et al* combined the four BCG constructs in a single inoculum, and the results reflected the combined effect of the four, not nef alone (3rd paragraph, page 95). Moreover, *Leung et al* only examined cellular and humoral immune responses induced, and did not teach whether such immune response is associated with a protective immune response, which is required for evaluating a vaccine. As indicated by numerous teaching in the field (e.g. *Allen* April 2002 and *Allen* Oct. 2002), including *Leung et al*, inducing an immune response, even a CTL response, often does not correlates with a protective effect for HIV/SIV viral infection (e.g. 2nd paragraph, page 95).

c. As with *Leung et al*, *Ayyavoo et al* made attenuated HIV-1 accessory gene expression construct, induced immune response *in vitro* and *in vivo*, but fails to teach such responses would lead to a protection on HIV/SIV viral infection.

d. *Ciernik et al* teach using an antigenic epitope for genetic tumor vaccine, they did not show that the epitope asserted any effect on HIV/SIV viral infection.

e. *Allen et al* (Oct. 2002) tested immunodominant gag epitope, which induced strong CTL response. Yet again, *Allen et al* reported, "BY THEMSELVES, THESE STRONG CTL RESPONSES FAILED TO CONTROL SIVMAC239 REPLICATION" (e.g. abstract), this illustrated the dissociation between the immune response induced by the HIV/SIV proteins and the vaccination.

Allen et al cannot be used to support the parts of the gag protein, also because it was published after the effective filing date, and the parts was not available at the time of the instant priority date.

f. *Allen et al* (April 2002) teach Tat-based vaccine does not control SIV replication, yet again pointing to the non-enablement of instantly claimed invention.

g. *Subbramanian* (Sep 2003) reference cannot be used to support the parts of the gag protein, because it was published after the effective filing date, and the parts was not available at the time of the instant priority date, nor any epitope was taught by the instant disclosure.

Moreover, in a survey published five years after instant priority date, *Yu et al* (Curr Medicinal Chemistry 2005;12:741-7) review the state of the art using regulatory and accessory HIV-1 proteins as potential targets for HIV-1 vaccine, which include Rev, Tat, Vpr, Vpu, Vif as recited in the instant claims. *Yu et al* teach these accessory proteins are essential for efficient viral replication, but only limited data is available

evaluating the role of immune response directed against these proteins in natural HIV-1 infection and in vaccine development (abstract). *Yu et al* indicates, "MOST OF THE VACCINES DEVELOPED TO DATE AGAINST HIV-1, SIV OR CHIMERIC SHIV VIRUSES HAVE INCLUDED THE VIRAL STRUCTURAL GAG, ENV AND A PART OF POL GENES OR GENE PRODUCTS. THESE VACCINES, HOWEVER, HAVE NOT PROVIDED PROTECTION FROM INFECTION, ALTHOUGH IN SOME CASES, A SLOWER PROGRESSION TO DISEASE WAS OBSERVED" (column 1, page 745). *Yu et al* cited studies showing possible benefits of including regulatory and accessory proteins as part of a vaccine, but they were published *after* the instant filing date (see page 743, cited references 7, 8, 13, 14, 17, 56-58). Thus, it is clear the state of the art at the time of instant filing was not well developed for the role of the accessory proteins of AIDS viruses. Therefore, it is incumbent upon applicants to provide sufficient and enabling teachings within the specification for the claimed invention. Although the instant specification contemplated using such regulatory and accessory molecules as vaccine components, it is not enabled for the claimed full scope because the specification fails to show these proteins are indeed capable of providing any beneficial effect for preventing or treating AIDS. Therefore, the general knowledge and levels of skill in the art do not supplement the omitted disclosure, and the specification fails to meet the enablement requirement for the full scope of the claims.

The newly submitted claims require the use of a processed product for vaccine of immunodeficiency viruses. However, the claims and specification fails to teach the structure of the processed product, one would not know how to make and use the invention.

Concerning the parts of a HIV/SIV protein, Applicant asserted that pages 22-23 of the specification provides specific exemplary parts of a pol, gp41, tat, rev, vap, vpx vpr vif nef gag or gag-pol fusion protein, and unambiguously informs skilled artisans of the parts of these proteins.

In response, the applicant is reminded that the central issue is whether the HIV/SIV proteins and the parts thereof have the capability of serving as a vaccine for HIV/SIV. As discussed previously, although it is known in the art that the HIV viral proteins could be cleaved and truncated to many parts (fragments), it is not fully developed and often controversial in the art concerning which parts of the protein has the capability to induce a meaningful and protective immune response against HIV/SIV to such extent that it serves as a vaccine. Moreover, it is noted that pages 22-23 of the specification provides discussion regarding exemplary parts of the gag and env proteins, but not the rest of the recited proteins, and it does not provide the teaching regarding the immunogeneicity of the HIV/SIV proteins and the discussed parts. Thus the specification fails to provide adequate disclosure on this matter, and thus fails to meet the requirement under this provision.

Accordingly, for reasons of record and set forth *supra*, the specification fails to provide adequate support to enable the full scope of instant claims, and the rejection stands.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 67-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite because of the claim recitation "wherein the part is a **processed product**". Since the specification fails to define what the phrase "a processed product" encompasses and excludes, the meaning of the phrase is unclear in the context of the claims, and the metes and bounds of the claims are uncertain.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 4, 16-19, stand rejected and claims 65, 66 are newly rejected under 35 U.S.C. 103(a) as being obvious over *Nagai et al* (US 7,101,685), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hirsch et al* (J Virol 1996;3741-52), for reasons of record and following.

Claims 65 and 66 are directed to a sendai virus vector encoding a gag protein, which has been addressed by the cited reference of *Hirsch et al.*

Applicants indicated they would address this rejection upon an indication of allowable subject matter. Until then, the rejection stands for reasons of record.

Claim 69 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Nagai et al* (US 7,101,685), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hirsch et al* (J Virol 1996;3741-52) as applied to claims 2, 4, 16-19, 65, 66 above, and further in view of *Hanke et al* (Vaccine 1999;17:586-96).

Although the combined teachings of *Nagai et al* in view of *Yu et al* and *Hirsch et al* do not specify expressing an epitope of an HIV antigen, the state of the art as illustrated by *Hanke et al* indicated it would have been obvious for the skilled artisan to make a vector construct for expressing either a full length protein or an epitope thereof for developing a genetic AIDS vaccine. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 2, 4, 5, 7, 9, 16-20, 24, 26, 28-33, 37, 39, 41-45, 62-66, 68-72 stand or newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), *Seth et al* (PNAS 1998;95:10112), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Hurwitz et al* (Vaccine 1997;15:533-40); and as evidenced by *Ourmanov et al* (J Virol 2000;74:2740-51, IDS), *Hanke et al* (Vaccine 1999;17:586-96), and *Nakanishi et al* (J Controlled Release 1998;54:61-8), for reasons of record and following.

Flanagan et al teach using a recombinant adenovirus expressing SIV Gag protein for vaccination in mice by intranasal inoculation, and teach that mucosal route of delivery is desirable for inducing a cellular immune response. *Seth et al* teach administering a recombinant vaccinia virus vector expressing gag-pol fusion

polypeptides in multiple dosages (day 1 and 126) and inducing cytotoxic immune response specific to gag pol proteins in a rhesus monkey. *Ourmanov et al* evidenced that VV-gag-pol vaccine (as used by *Seth et al*) indeed provided protection from high levels of viremia and AIDS following challenge with a pathogenic strain of SIV in macaques.

Claims 68-71 are drawn to a part of an immunodeficiency viral protein that is an epitope. *Seth et al* teach that cytotoxic T lymphocytes are important in containing the spread of HIV-1 in infected individuals, and the induction of a specific CTL response generally requires just a short peptide in association with a MHC class I molecule (e.g. column 1, page 10112). Although not relied upon, *Hanke et al* have shown using multi-epitope strategy for inducing HIV-specific CTL for vaccination.

The teachings of *Flanagan et al* and *Seth et* al established the state of the art in developing genetic vaccines for AIDS, although they did not teach a particular vector, sendai viral vectors, *Yu et al* cured the deficiency. *Yu et al* supplemented the teaching of *Flanagan et al* and *Seth et al* by establishing the advantage of using sendai virus, particularly V(-) sendai virus as a expression vector in expressing a HIV protein, and its expression efficiency in cells that are natural hosts for AIDS virus. *Yu et al* teach the need for establishing a better system to express HIV antigen in natural host cells for HIV such as human primary blood mononuclear cells, macrophages or T cells (e.g. abstract), and compared the V- SeV with the commonly used *vaccinia virus vector* that was used by *Seth*, and teach "THE V(-) VERSION APPEARS TO BE EXCELLENT AND ALMOST COMPARABLE TO THE ABOUVE NOTED VV-BASED EXPRESSION" (column 1, page 462, emphasis

added). Clearly, *Yu et al* teach that sendai virus could be used as a gene transfer vector for expressing a nonanalogous viral protein, such as the immunodeficiency virus protein, in place of the vaccinia virus or interchangeably with other known viral vectors. *Yu et al* further teach the advantages of a V(-)SeV such as a robust heterologous gene expression capability in mammalian cells, moderate pathogenesis, and broad host range.

Hurwitz et al supplemented the combined teaching by establishing the feasibility of sendai virus nasal inoculation. *Hurwitz et al* teach nasal inoculation of sendai virus is non-pathogenic for primates. *Hurwitz et al* also teach the effectiveness of intranasal multiple inoculation (abstract, figures 1-4, and table 1). *Hurwitz et al* go on to teach the advantage of using Sendai virus as a potential human vaccine because its long-lasting effect stimulating memory B-cells as well as CTL response (last paragraph, page 539).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Flanagan et al* or *Seth et al*, by substituting and/or combining the recombinant adenoviral or vaccinia vector with a Sendai viral vector as taught by *Yu et al*, for expressing an immunodeficiency virus protein or an epitope thereof, and delivering such via intranasal inoculation as taught by *Flanagan* et al, and *Hurwitz et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention given the knowledge that the V(-) sendai virus vector could efficiently expressing an HIV antigenic protein in natural host cells for immunodeficiency virus, and given numerous carrier vectors known and used in the art, and all proven to be effective in expressing a

viral protein at sufficient levels. Thus, the limitation falls within the bound of optimization for the skilled artisan to determine which vector would serve their goal the best.

Response to Arguments

In the remarks, applicant argued that the claims has been amended to recite "Sendai virus gene-transfer vector" in place of "Sendai virus vector", while *Yu et al* disclose the use of Sendai virus as *an expression vector.*

In response, as an initial matter, although the specification as filed teaches the use of a sendai virus vector for gene transfer, it fails to make a distinction for the structural differences between [a sendai virus] "expression vector" and "gene transfer vector".

In view of the state of the art at the time of the priority date, gene transfer by a viral vector is closely associated and measured by the levels of transgene expression, and there is no clear distinction between a gene transfer vector and an expression vector. For example, *Nakanishi et al* (J Controlled Release 1998;54:61-8) teach "WE MUST BE ABLE TO DELIVER GENES [gene transfer] EFFICIENTLY IN SITU AND INDUCE STABLE GENE EXPRESSION IN NON-DIVIDING CELLS" (abstract, emphasis added). It is a common knowledge in the art that gene transfer is practiced with an expression vector in applications of gene therapy and genetic vaccination (immunological studies). Thus the mere recitation of "gene-transfer" dose not change the structure of the claimed sendai virus vector nor distinguishing such from the vector taught by *Yu et al.*

Moreover, the fact that *Yu et al* teach the expression efficiency of a transgene by the V(-) sendai virus does not negate the fact that the vector could be used for gene transfer. To the contrary, *Yu et al* stressed the usefulness of the vector in expressing transgene in a wide variety of mammalian cells, and compared the sendai viral vector with the gene transfer vector taught by *Seth et al,* which indicates that *Yu et al* is fully aware the use of a V(-) sendai virus vector for gene transfer.

Applicant then argued that nothing is disclosed about Sendai virus vector in *Flanagan*, and *Seth*. In response, the missing teaching is remedied by *Yu et al* and *Hurwitz et al.*

Applicant then argue that Hurwitz et al do not disclose or suggest the use of sendai virus as a gene-transfer vector encoding and expressing a heterologous viral protein. In response, such is taught by *Yu et al. Hurwitz et al* was cited to show the desirability and the feasibility of intranasal multiple inoculation of a Sendai virus in primates.

Applicant went on to argue "although Yu et al describe the foreign gene insertion site in Sendai virus, a luciferase gene inserted in the insertion site was overexpressed and the expression product was aggregated so as not to be functional". Thus from the teaching of Yu et al, it is questionable whether a Sendai virus vector encoding a foreign gene could produce a foreign gene product that is functional to induce an immune response specific to the product.

In response, it is noted *Yu et al* clearly teach the HIV-gp120 expressed by the sendai virus vector is "FUNCTIONALLY AND ANTIGENECALLY AUTHENTIC" (column 2, page 458).

As to the luciferase product, *Yu et al* cited *Hasan et al* (J Gen Virol 1997;78:2813-20) reference, and indicated the aggregation of the luciferase made it difficult to measure the amount of protein production, which is not to say the product is not functional. Indeed, *Hasan et al* teach measuring the luciferase enzyme activity (c.p.s.) by a luminometer (e.g. page 2814), and state, "A RECOMBINANT SEV EXPRESSING LUCIFERASE ACTIVITY AT A HIGH LEVEL WAS RECOVERED, ALTHOUGH THE TENDENCY OF THIS PARTICULAR REPORTER GENE PRODUCT TO AGGREGATE IN CELLS MADE IT DIFFICULT TO ESTIMATE THE MAXIMUM LEVEL OF EXPRESSION", "THE INSERTED LUCIFERASE GENE WAS STABLY MAINTAINED AFTER NUMEROUS ROUNDS OF REPLICATION BY SERIAL PASSAGES IN CHICK EMBRYOS. THESE RESULTS INDICATE THE POTENTIAL UTILITY OF SEV AS A NOVEL EXPRESSION VECTOR" (e.g. abstract and fig. 2). Accordingly, the product produced by the vector taught by *Yu et al* not only highly efficient but also functional.

Accordingly, for reasons of record and set forth *supra*, the rejection stands.

Claims 11-13 and 15 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Kast et al* (J Immunol 1988;140:3186-93, IDS), for reasons of record and *supra*.

Flanagan et al teach the *in vitro* CTL assay, wherein a recombinant viral vector encoding a gag protein is introduced to APCs (splenocytes, stimulator cells), which then incubated (contact) with splenocytes of immunized mice, which splenocytes comprise T

helper and T cytotoxic cells (responders), and a cellular immune response specific to a SIV gag is induced (CTL-assays, page 992).

The method of *Flanagan et al* differs from instant claimed in that they did not use a sendai viral vector expressing the HIV/SIV protein, *Yu et al* supplemented the teaching of *Flanagan et al* by establishing it was well known in the art to use a sendai viral vector expressing an immunodeficiency virus protein at a high level and in all three natural host cells for HIV-1. It would have been obvious for the skilled in the art to use one of the art known vectors in the CTL assay or expressing H/SIV in its natural host cells with a reasonable expectation of success.

The teaching of *Kast et al* supplemented *Flanagan et al* in view of *Yu et al* by establishing the infectivity of the sendai virus in antigen-presenting cells. *Kast et al* extensively discussed how to use the sendai virus infected dendritic cells (APC) in the CTL assay to measure an in vivo immune response (left column, page 3187), to test the activity of T helper and cytotoxic T lymphocytes.

It is noted each CTL assay in the cited references may slightly differ in the type of antigen presenting cells, the source of Th and $T_{cytotoxic}$ cells, but these are the obvious alternatives and variants well known to the ordinary skilled in the art.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Flanagan et al* and *Kast et al*, by employ the vector taught by *Yu et al* with a reasonable expectation of success in inducing a specific cellular immune response for an immunodeficiency virus protein. The ordinary skilled artisan would have been motivated to modify the method for their

particular needs of investigation, i.e. a particular disease of interest, or a particular antigen of interest, etc. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claim 14 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Kast et al* (J Immunol 1988;140:3186-93, IDS) as applied to claims 11-13, and 15 above, further in view of *Boutillon et al* (US 6,015,564), for reasons of record and *supra*.

Claim 67 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Flanagan et al* (J Gen Virol 1997;78:991-7), in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), and *Kast et al* (J Immunol 1988;140:3186-93, IDS) as applied to claims 11-13, and 15 above, further in view of *Hanke et al* (Vaccine 1999;17:589-96).

The combined teachings of *Flanagan et al* in view of *Yu et al* and *Kast et al* do not specify using an epitope of an immunodeficiency virus for inducing CTL response.

Hanke et al supplemented the deficiency by establishing the knowledge in the art concerning using antigenic epitopes for inducing an HIV-specific CTL response. *Hanke et al* teach by using multiple CTL-epitopes, one can induce strong and reliable CTL-response for developing HIV vaccine.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Flanagan et al* in view of *Yu et al*

and *Kast et al*, by expressing one of more epitopes in place of a full length protein as taught by *Hanke et al* with a reasonable expectation of success in inducing a specific cellular immune response for an immunodeficiency virus protein. The ordinary skilled artisan would have been motivated to modify the method for a strong and stable anti-HIV response. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2, 4, 16-19, 65, 66, 69 stand or newly rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 5, 13 of copending Application No. 09/728,207, now U.S. patent 7,101,685, in view of *Yu et al* (Genes Cells. 1997 Jul;2:457-66), *Hirsch et al* (J Virol 1996;3741-52), and *Hanke et al* (Vaccine 1999;17:589-96) for reasons of record and *supra*.

Applicants request that the provisional rejection be held in abeyance until such time as allowable subject matter is identified.

Until then, for reasons of record, the rejection stands.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Dave T. Nguyen** can be reached on 571-272-0731. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Victor Barlow**, whose telephone number is (571) 272-0506.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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PRIMARY EXAMINER

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QJL
September 5, 2006